IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)
KOLTER et al.) Applications
)
)
Serial No. Not Assigned)
)
Filed:)
)

For: A PROCESS FOR PRODUCING SOLID ORAL DOSAGE FORMS WITH SUSTAINED RELEASE OF ACTIVE INGREDIENTS

PRELIMINARY AMENDMENT

Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

Prior to examination, kindly amend the above-identified application as follows.

IN THE CLAIMS

Please amend the claims as shown in the attached sheets.

REMARKS

The claims have been amended to eliminate multiple dependency. No new matter has been added. A clean copy of the claims is attached.

Entry of the above amendment is respectfully solicited.

Respectfully submitted,

KEIL & WEINKAUF

/HBKeil

Herbert B. Keil
Reg. No. 18,967

1101 Connecticut Ave., N.W.
Washington, D.C. 20036
(202)659-0100

3. A process as claimed in claim 1 [either of claim 1 or 2], wherein the active ingredient : release-slowing agent ratio employed in the combination is from 5:95 to 85:15.

4. A process as claimed in claim 1 [any of claims 1 to 3], wherein polyvinyl acetate and polyvinylpyrrolidone each have a molecular weight of from 20,000 to 1,000,000.

5. A process as claimed in claim 1 [any of claims 1 to 4], wherein the mixture is granulated by heating to from 45 to 100°C.

6. A process as claimed in claim 1 [any of claims 1 to 5], wherein the particle size of the active ingredients employed is in a range from 20 to 700 µm.

7. A process as claimed in claim 1 [any of claims 1 to 6], wherein the conventional excipients employed are fillers, disintegrants and adsorbents, lubricants, flowability agents, dyes, stabilizers, antioxidants, wetting agents, preservatives, release agents, flavorings or sweeteners.

8. A process as claimed in claim 1 [any of claims 1 to 7], wherein fillers such as lactose, cellulose powder, mannitol, calcium diphosphate or starch are employed as excipients.

9. A process as claimed in claim 1 [any of claims 1 to 8], wherein the granules can be produced by employing the process of mixer granulation, fluidized bed granulation or extrusion granulation.

10. A process as claimed in claim 1 [any of claims 1 to 9], wherein production is possible both continuously and batchwise.

11. A process as claimed in claim 1 [any of claims 1 to 10], wherein further processing of the granules, principally the forced screening, can take place both in the hot state and in the cooled state.

12. A process as claimed in claim 1 [any of claims 1 to 11], wherein besides the formulated mixture of polyvinyl acetate and polyvinylpyrrolidone, it is possible to employ further release-sustaining excipients before, during or after the granulation.

13. A process as claimed in claim 1 [any of claims 1 to 12], wherein water-soluble, water-soluble highly swelling or lipophilic excipients are employed for further modification of release.

14. A process as claimed in claim 1 [any of claims 1 to 13], wherein the water-soluble highly swelling substances employed are alginates, pectins, galactomannans, carrageenans, dextran, curdlan, pullulan, gellan, chitin, gelatin, xanthans, hemicelluloses, cellulose derivatives such as methylcellulose, hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxyethylcellulose, carboxymethylcellulose, starch derivatives such as carboxymethylstarch, degraded starch, maltodextrins, polyacrylic acid, polymethacrylic acid, acrylic acid/methacrylic acid copolymers, polyvinyl alcohols, high molecular weight polyethylene glycols, polyoxyethylene/polyoxypropylene block copolymers, high molecular weight polyvinylpyrrolidones and derivatives thereof.

15. A process as claimed in claim 1 [any of claims 1 to 13], wherein the lipophilic substances employed are fatty alcohols such as stearyl alcohol, fatty acids such as

stearic acid, glycerides, fatty acid esters and fatty alcohol esters, lipophilic polymers such as ethylcellulose, cellulose acetate, acrylic ester/methacrylic ester copolymers, methacrylic acid/acrylic ester copolymers, cellulose acetate phthalate, cellulose acetate succinate, hydroxypropylmethylcellulose acetate phthalate, hydroxypropylmethylcellulose acetate succinate and derivatives thereof.

16. A process as claimed in claim 1 [any of claims 1 to 13], wherein the water-soluble polymers are selected from the group of: polyvinyl alcohols, polyethylene glycols, polyoxyethylene/polyoxypropylene block copolymers, polyvinylpyrrolidones and derivatives, vinyl acetate/vinyl pyrrolidone copolymers, preferably polyethylene glycols, polyvinylpyrrolidones, vinyl acetate/vinylpyrrolidone copolymers or maltodextrins, and salts thereof.

19. An oral dosage form as claimed in claim 17 [either of claim 17 or 18], which comprises active pharmaceutical ingredients as active ingredients.

20. An oral dosage form as claimed in claim 17 [any of claims 17 to 19], wherein the active pharmaceutical ingredient is selected from the group of benzodiazepines, antihypertensives, vitamins, cytostatics, anesthetics, neuroleptics, antidepressants, antibiotics, antimycotics, fungicides, chemotherapeutics, urologicals, platelet aggregation inhibitors, sulfonamides, spasmolytics, hormones, immunoglobulins, sera, thyroid therapeutics, psychopharmaceuticals, antiparkinson agents and other antihyperkinetics, ophthalmologicals, neuropathy products, calcium metabolism regulators, muscle relaxants, lipid-lowering agents, liver therapeutics, coronary agents,

cardiac agents, immunotherapeutics, regulatory peptides and their inhibitors, hypnotics, sedatives, gynecologicals, antigout agents, fibrinolytics, enzyme products and transport proteins, enzyme inhibitors, emetics, perfusion promoters, diuretics, diagnostics, corticoids, cholinergics, biliary therapeutics, antiasthmatics, bronchospasmolytics, beta-receptor blockers, calcium channel blockers, ACE inhibitors, arteriosclerosis remedies, antiinflammatory agents, anticoagulants, antihypotensives, antihypoglycemics, antifibrinolytics, antiepileptics, antiemetics, antidotes, antidiabetics, antiarrhythmics, antianemics, antiallergics, anthelmintics, analgesics, analeptics, aldosterone antagonists, weight-reducing agents.

21. An oral dosage form as claimed in claim 17 [any of claims 17 to 20], which is used to produce compressed tablets.

22. A drug product with delayed release of active ingredient, which is an oral dosage form as claimed in claim 17 [any of claims 17 to 20].

23. A drug product for delayed release of active ingredient, which is an oral dosage form as claimed in claim 17 [any of claims 17 to 20] which has been produced by compression.

24. The use of the oral dosage forms as claimed in claim 17 [any of claims 17 to 20] for producing drug products with delayed release of active ingredient.

25. The use of the oral dosage forms as claimed in claim 17 [any of claims 17 to 20] for the delayed release of active ingredients in the form of food supplements or additives, vitamins, minerals or trace elements.

CURRENT CLAIMS - OZ 51497

1. A process for producing an oral dosage form with sustained release of active ingredient, comprising

   a) a formulated mixture of polyvinyl acetate and polyvinylpyrrolidone

   b) at least one active ingredient

   c) where appropriate water-soluble polymers or low or high molecular weight lipophilic additives

   d) and, where appropriate, other conventional excipients,

   wherein the mixture of a) to d) or a) to c) or a) and b) and d) or a) and b) is granulated by heating to from 40%C to 130%C.

2. A process as claimed in claim 1, wherein the polyvinyl acetate to polyvinylpyrrolidone ratio is from 6:4 to 9:1.

3. A process as claimed in claim 1, wherein the active ingredient : release-slowing agent ratio employed in the combination is from 5:95 to 85:15.

4. A process as claimed in claim 1, wherein polyvinyl acetate and polyvinylpyrrolidone each have a molecular weight of from 20,000 to 1,000,000.

5. A process as claimed in claim 1, wherein the mixture is granulated by heating to from 45 to 100°C.

6. A process as claimed in claim 1, wherein the particle size of the active ingredients employed is in a range from 20 to 700 µm.

7. A process as claimed in claim 1, wherein the conventional excipients employed are fillers, disintegrants and adsorbents, lubricants, flowability agents, dyes, stabilizers, antioxidants, wetting agents, preservatives, release agents, flavorings

or sweeteners.

8. A process as claimed in claim 1, wherein fillers such as lactose, cellulose powder, mannitol, calcium diphosphate or starch are employed as excipients.

9. A process as claimed in claim 1, wherein the granules can be produced by employing the process of mixer granulation, fluidized bed granulation or extrusion granulation.

10. A process as claimed in claim 1, wherein production is possible both continuously and batchwise.

11. A process as claimed in claim 1, wherein further processing of the granules, principally the forced screening, can take place both in the hot state and in the cooled state.

12. A process as claimed in claim 1, wherein besides the formulated mixture of polyvinyl acetate and polyvinylpyrrolidone, it is possible to employ further release-sustaining excipients before, during or after the granulation.

13. A process as claimed in claim 1, wherein water-soluble, water-soluble highly swelling or lipophilic excipients are employed for further modification of release.

14. A process as claimed in claim 1, wherein the water-soluble highly swelling substances employed are alginates, pectins, galactomannans, carrageenans, dextran, curdlan, pullulan, gellan, chitin, gelatin, xanthans, hemicelluloses, cellulose derivatives such as methylcellulose, hydroxypropylmethylcellulose,

hydroxypropylcellulose, hydroxyethylcellulose, carboxymethylcellulose, starch derivatives such as carboxymethylstarch, degraded starch, maltodextrins, polyacrylic acid, polymethacrylic acid, acrylic acid/methacrylic acid copolymers, polyvinyl alcohols, high molecular weight polyethylene glycols, polyoxyethylene/polyoxypropylene block copolymers, high molecular weight polyvinylpyrrolidones and derivatives thereof.

15. A process as claimed in claim 1, wherein the lipophilic substances employed are fatty alcohols such as stearyl alcohol, fatty acids such as stearic acid, glycerides, fatty acid esters and fatty alcohol esters, lipophilic polymers such as ethylcellulose, cellulose acetate, acrylic ester/methacrylic ester copolymers, methacrylic acid/acrylic ester copolymers, cellulose acetate phthalate, cellulose acetate succinate, hydroxypropylmethylcellulose acetate phthalate, hydroxypropylmethylcellulose acetate succinate and derivatives thereof.

16. A process as claimed in claim 1, wherein the water-soluble polymers are selected from the group of: polyvinyl alcohols, polyethylene glycols, polyoxyethylene/polyoxypropylene block copolymers, polyvinylpyrrolidones and derivatives, vinyl acetate/vinyl pyrrolidone copolymers, preferably polyethylene glycols, polyvinylpyrrolidones, vinyl acetate/vinylpyrrolidone copolymers or maltodextrins, and salts thereof.

17. An oral dosage form comprising

a) a formulated mixture of polyvinyl acetate and polyvinylpyrrolidone

b) at least one active ingredient

c) where appropriate water-soluble polymers or low or high molecular weight lipophilic additives

d) and, where appropriate, other conventional excipients,

wherein the mixture of a) to d) or a) to c) or a) and b) and d) or a) and b) is granulated by heating to from 40%C to 130°C.

18. An oral dosage form as claimed in claim 17, which comprises as active ingredients food supplements or additives, vitamins, minerals or trace elements or active pharmaceutical ingredients.

19. An oral dosage form as claimed in claim 17, which comprises active pharmaceutical ingredients as active ingredients.

20. An oral dosage form as claimed in claim 17, wherein the active pharmaceutical ingredient is selected from the group of benzodiazepines, antihypertensives, vitamins, cytostatics, anesthetics, neuroleptics, antidepressants, antibiotics, antimycotics, fungicides, chemotherapeutics, urologicals, platelet aggregation inhibitors, sulfonamides, spasmolytics, hormones, immunoglobulins, sera, thyroid therapeutics, psychopharmaceuticals, antiparkinson agents and other antihyperkinetics, ophthalmologicals, neuropathy products, calcium metabolism regulators, muscle relaxants, lipid-lowering agents, liver therapeutics, coronary agents, cardiac agents, immunotherapeutics, regulatory peptides and their inhibitors, hypnotics, sedatives, gynecologicals, antigout agents, fibrinolytics,

enzyme products and transport proteins, enzyme inhibitors, emetics, perfusion promoters, diuretics, diagnostics, corticoids, cholinergics, biliary therapeutics, antiasthmatics, bronchospasmolytics, beta-receptor blockers, calcium channel blockers, ACE inhibitors, arteriosclerosis remedies, antiinflammatory agents, anticoagulants, antihypotensives, antihypoglycemics, antifibrinolytics, antiepileptics, antiemetics, antidotes, antidiabetics, antiarrhythmics, antianemics, antiallergics, anthelmintics, analgesics, analeptics, aldosterone antagonists, weight-reducing agents.

21. An oral dosage form as claimed in claim 17, which is used to produce compressed tablets.

22. A drug product with delayed release of active ingredient, which is an oral dosage form as claimed in claim 17.

23. A drug product for delayed release of active ingredient, which is an oral dosage form as claimed in claim 17 which has been produced by compression.

24. The use of the oral dosage forms as claimed in claim 17 for producing drug products with delayed release of active ingredient.

25. The use of the oral dosage forms as claimed in claim 17 for the delayed release of active ingredients in the form of food supplements or additives, vitamins, minerals or trace elements.